UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Chemical name: Difenoconazole
PC Code: 128847
DP Barcode: D252640

MEMORANDUM

SUBJECT: Ecological Risk Assessment for Section 3 Registration of Difenoconazole as Seed Treatment on Canola

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I. Environmental Risk Conclusions

Novartis has applied for registration of the fungicide difenoconazole as a seed treatment for use on canola. The proposed use does not pose acute or chronic risk to aquatic organisms nor acute risk to birds and mammals. However, the proposed use indicates a possible chronic risk to both mammals and birds. Risk to terrestrial and aquatic plants was not evaluated due to the lack of plant toxicity data.

Difenoconazole is expected to be relatively immobile and persistent in terrestrial environments. No surface water or ground water monitoring data were available for difenoconazole. To simulate

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the concentration of difenoconazole in surface drinking water, the GENEEC model using the maximum annual wheat application rate of 0.03lb ai/acre was utilized. Predicted concentrations of difenoconazole in drinking water were 0.120 µg/L (acute) and 0.045 µg/L for the 56-day average concentration (chronic). Based on the wheat application rate, SCI-GROW modeling estimated the concentration of difenoconazole in drinking water from shallow ground water sources to be 0.0012 µg/L.

GENEEC modeling for the canola use, estimated the concentrations of difenoconazole in surface water to be 0.0077 µg/L (acute), 0.0044 µg/L (21-day chronic) and 0.0029 µg/L (56-day chronic).

Since GENEEC and SCI-GROW are not designed to estimate runoff or leaching for seed treatment pesticides, there are uncertainties in the predictive potential of the Tier 1 modeling for drinking water assessment.

Data requirement Gaps:

This assessment was based on submitted acceptable and supplemental data. The following fate data requirements remain unsatisfied but some studies provide sufficient information to conduct this risk assessment:

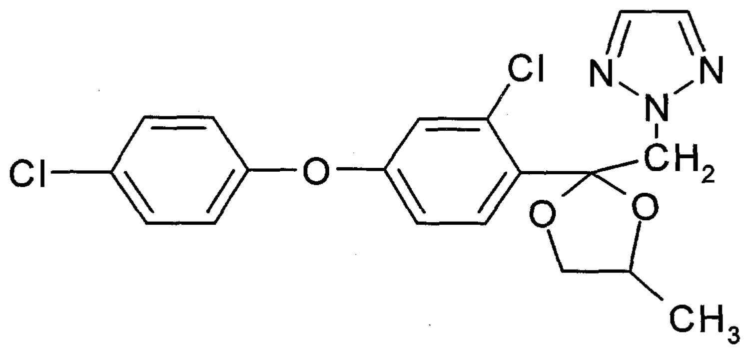
1- Aqueous Photolysis (161-2)
2- Photodegradation on soil (161-3)
3- Aerobic Soil Metabolism (162-1)
4- Anaerobic Soil Metabolism (162-2)
5- Anaerobic aquatic metabolism (162-3)
6- Aerobic Aquatic metabolism (162-4)
7- Leaching and Adsorption Desorption Studies 163-1
8- Laboratory Volatility from Soil (163-2)
9- Field Volatility (163-3)
10- Terrestrial Field Dissipation Studies (164-1)

The following toxicity data are not satisfied:

1- Avian reproduction (71-4)
2- Early life stage fish (72-4a)
3- Life cycle aquatic invertebrate(72-4b)
4- Seed germ./seedling emergence (122-1a)
5- Vegetation vigor (122-1b)
6- Aquatic plant growth (122-2)

Chemical Profile

Common Name: Difenoconazole
Trade Name: Dividened XL, Dividened XL RTA
Chemical Name: 1-{2-[4-(chlorophenoxy)-2-chlorophenyl-(4-methyl -1,3-dioxolan-2-yl)-methyl]}-1H-1,2,4-triazole
Chemical Class: Triazole Fungicide
Chemical Structure:



Physical/Chemical Properties:
Molecular Formula: $C_{19}H_{17}Cl_2N_3O_3$
Molecular Weight : 406.27
Physical State : Red Liquid
Specific Gravity/Density: 1.14 g/cm^3 @ 25^0 C
Vapor Pressure : 3.32E-05 mPA @ 25^0 C
Water Solubility : 15.0 mg/L @ 25^0 C
CAS Number : 119446-68-3
PC Code: 128847

II. Integrated Environmental Risk Characterization

Aquatic Risk Assessment

The proposed use of difenconazole on canola is not expected to pose a significant acute or chronic risk to aquatic organisms. No acute or chronic levels of concern (LOCs) were exceeded for freshwater fish and invertebrates and no acute LOC's were exceeded for marine/estuarine fish. Chronic RQ's could not be calculated for marine/estuarine invertebrates due to the lack of valid toxicity data.

Terrestrial Risk Assessment

Acute risk quotients calculated for granivorous birds consuming treated seed were below all EFED acute risk levels of concern. However, the chronic RQs suggest a possible chronic risk to birds, with an RQ of 1.92 exceeding the LOC of 1.0.

Similar to birds, the calculated RQs for granivorous mammals were well below acute risk levels of concern. However, the chronic RQs calculated for this use of Difenoconazole suggest a potential for reproduction effects, with an RQ of 9.6 exceeding the EFED chronic level of concern (1.0).

Difenoconazole is classified as relatively non-toxic to beneficial insects such as honey bees. Risk to terrestrial plants was not evaluated due to the lack of plant toxicity data.

Uncertainties in the Terrestrial Risk Assessment

There are a number of uncertainties in the avian and mammalian risk assessments that include the following:

1. **Only dietary exposure is included in the exposure assessment.** Other exposure routes are possible for birds in treated areas. These routes include ingestion of contaminated drinking water, ingestion of contaminated soils, preening, dermal contact, and inhalation. Consumption of drinking water would appear to be inconsequential if water concentrations were equivalent to the low concentrations from GENEEC and SCI-GROW. However, if difenoconazole does not readily sorb to the seed coat, concentrations in puddles in the planted field could be expected to be higher, and so the drinking water route remains an unquantified concern. Similarly, consumption of soil and grit from the treated field would pose low risk if difenoconazole sorbs to the seed coat. Given the high affinity for organic carbon and the pesticide's intended use to control fungal growth on seeds, it is unlikely that the compound disassociates from the seed to a great extent.

   Dermal contact is not likely to be a great contributor to overall pesticide load to wildlife because of the seed treatment method of application. Because difenoconazole does not volatilize appreciably (v.p. 3.3×10^{-5} mm Hg at 25°C), inhalation does not appear to be a significant contributor to overall exposure.

   Preening exposures, involving the oral ingestion of material from the feathers remains an unquantified, but potentially important, exposure route.

2. **The risk assessment only considers the most sensitive species tested**. Avian acute and chronic risks are based on toxicity data for the most sensitive bird species tested. Responses to a toxicant can be expected to be variable across species. In the case of difenoconazole, only two bird species have been tested. Sensitivity differences between

species can be considerable (up to two orders of magnitude) for some chemicals. It is therefore possible that more sensitive species exist in the field than have been tested. Likelwise it is possible that there are less sensitive species extant in the field as well.

3. **The risk assessment assumes 100% of the diet is relegated to a single food type foraged only from treated fields.** These assumptions are likely to be conservative for many species. The assumption of 100% diet from a treated area may be realistic for acute exposure. However, fort longer-term exposures that are consistent with observations of reproductive effects in birds and mammals, modeling exposure from a single food source composed entirely of material from a treated field is uncertain. Based on the small size of the canola seed and the shallow planting depth, EFED made the conservative assumption that at least some of the treated seed would be available and would constitute 100% of the diet. While these assumptions are conservative, canola is an attractive seed to birds and other wildlife. Seeds can comprise almost the entire diet of some species of small birds (e.g., redpolls, sparrows, and finches) during the late winter and early spring when canola is planted (Martin et al., 1951[1]). Martin et al. (1951) write of plants in the mustard family (like canola): "The oily seeds of these plants, often fed to cage birds, are relished by game birds and songbirds."

4. **Toxicity endpoints for reproductive effects and their relevancy to field effects.** EFED based chronic RQs in mammals on the no observable adverse effect level (NOAEL) for difenoconoazole in a 2-generation rat reproduction study. The observable effect associated with endpoint used in the risk assessment (1.25 mg/kg-bw/day or 25 mg/kg-diet) is weight reduction in pups. The NOAEL for decreased pup survival from this study was 12.5 mg/kg-bw/day or 250 mg/kg-diet. This latter endpoint is more consistent with the NOAEL observed for developmental effects (increases in post-implantation loss and resorptions) in rabbits (NOAEL 25 mg/kg-bw/day, MRID 42090017) and the NOAEL for developmental toxicity (100 mg/kg/day) based on increased skeletal abnormalities in rats (MRID 42090016). Using any of these higher NOAELs for more frank adverse effects would result in RQ calculations below EFED LOCs.

<u>Environmental Fate Assessment</u>

Based on acceptable and supplemental studies, difeneconazole is stable to hydrolysis at pH 5, 7, and 9. Difenoconazole is relatively stable to both aerobic and anaerobic soil metabolism. The calculated half-lives for parent difenoconazole in aerobic and anaerobic loam soil systems were 1600 days and 947 days, respectively. Difenoconazole photodegraded in water with a half-life of 6 days in sterilized pH 7 aqueous buffer solution. Leaching and adsorption/desorption studies indicate that difenoconazole is immobile in soil. Freundlich K_{ads} values were 12.8 for sand soil,

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[1]Martin, A. C., H. S. Zim, and A. L. Nelson. 1951. <u>American Wildlife and Plants: a guide to wildlife food habits.</u> New York: Dover Publications.

63.0 for sandy loam soil, 54.8 for silt loam soil, and 47.2 for silty clay loam soil. The corresponding K_{oc} values were 3867, 3518, 3471, and 7734 mL/g. Difenoconazole accumulated rapidly in edible and non-edible bluegill sunfish tissues with bioconcentration factors of 170x for edible tissues, 570x for nonedible tissues, and 330x for whole body. Depuration was also rapid with a depuration half-life of approximately 1 day and 96-98% clearance after 14 days of depuration.

III. Water Resources Summary

A. Surface Water

1) Ecological exposure

For the proposed use of difenoconazole as a seed treatment for canola, exposure concentrations for aquatic organisms were estimated using Tier 1 model GENEEC (Version 2.1, May 3, 1995). The model uses the soil/water partition coefficient and degradation half-life values to estimate runoff from a ten-hectare field into a one-hectare by two meter deep pond. The GENEEC estimated environmental concentrations from the use on canola are listed in table1.

Table 1. GENEEC Estimated Environmental Concentrations of Difenoconazole in Surface Water from the Seed Treatment Use on Canola

Crop	Application Rate (lbs. ai/acre)	Number of Applications	GENEEC Peak Conc. (µg/l)	GENEEC average 4 day Conc. (µg/l)	GENEEC average 21 day Conc. (µg/l)	GENEEC Average 56 day Conc. (µg/l)
Canola	0.00192 (based on 8 lbs. Seeding per acre)	1	0.0077	0.0069	0.0044	0.0029

(2) Drinking Water Concentration Estimates

The Tier 1 drinking water assessment was based on the use of difenoconazole as a wheat seed treatment. Since GENEEC is not designed to estimate runoff for seed treatment pesticides, there are uncertainties in the predictive potential of the Tier 1 modeling. The noted uncertainties in the water assessment, however, are not expected to substantially decrease the conservativeness of the Tier 1 modeling results.

The GENEEC model estimated the concentration of difenoconazole in drinking water from surface water sources to be **0.120 µg/L** for the maximum annual concentration (acute) and **0.045 µg/L** for the 56 day average concentration (chronic).

Uncertainties in the Modeling

The main uncertainty in the Tier 1 water assessment is the use of GENEEC and SCI-GROW models to estimate runoff and leaching of difenoconazole from seed treatment use. These models do not account for the pesticide sorption to the seed coat. For purposes of this assessment, it was assumed that defenconazole does not sorb to the seed coat and hence is simulating a broadcast applied pesticide. This assumption is expected to provide a conservative leaching and runoff scenario.

Other uncertainties in the model assessments are associated with the application rate of difenoconazole. The maximum seeding rate for wheat (120 lbs wheat seed/A) was used to calculate the maximum difenoconazole application rate. EFED notes that the planting rates for wheat can range from 60 to 120 lbs seed/A.

Input Parameter Selection

The application rate of difenconazole is based on a seed treatment rate of 0.025 lbs a.i./100 lbs (EPA Reg. No. 100-778) and of maximum seeding rate 120 lbs/A. Therefore, the maximum difenconazole application rate is 0.03 lbs ai/A.

Based on submitted environmental fate data, difenoconazole is expected to be relatively immobile and persistent in terrestrial environments. The adsorption coefficient for difenoconazole is 12.8 ml/g (K_{oc}=3867) in sand soil, 63.0 ml/g (K_{oc}= 3518) in sandy loam soil, 54.8 ml/g (K_{oc}=3471) in silt loam soil, and 47.18 ml/g (K_{oc}=7734) in a silty clay loam soil. The aerobic soil metabolism half-life for difenoconazole ranged from 175 to 1600 days. Difenoconazole had a first-order photodegradation in water half-life of 6 days. The GENEEC model input parameters for difenoconazole are shown in Table 2.

Table 2. GENEEC Input Parameters for the Use of Difenoconazole on Wheat		
MODEL PARAMETER	DATA SOURCE	VALUE
Application Rate On Wheat	Label EPA Reg# 100-788	0.03 lb ai/Acre (based on 120 lb seeding/Acre)
Maximum # of applications per year	Label EPA Reg# 100-788	One application
Hydrolysis $t_{1/2}$	42245127	Stable
Aerobic Soil Metabolism $t_{1/2}$	42245130	1600 days
Koc	42245135	4648 ml/g (mean value)
Solubility in Water	Material Safety Data Sheet (A-8574A)	15.0 mg/L @ 25°C
Aqueous Photolysis $t_{1/2}$	42245128	6 days

GENEEC estimated concentrations of difenoconazole in drinking water from surface water sources are shown in Table 3.

Table 3. GENEEC Estimated Concentrations of Difenoconazole in Drinking Water from Surface Water Sources.						
Crop	Application Rate (lbs. ai/acre)	Number of Applications	GENEEC Peak Conc. (µg/l)	GENEEC average 4 day Conc. (µg/l)	GENEEC average 21 day Conc. (µg/l)	GENEEC Average 56 day Conc. (µg/l)
Wheat	0.03	1	0.120	0.107	0.068	0.045

3) Monitoring

There are no surface water monitoring data readily available for difenoconazole. Difenoconazole was not analyzed under the National Water-Quality Assessment Program of the U.S. Geological Survey.

B. Ground Water

There are no ground water monitoring data readily available for difenoconazole. Difenoconazole was not listed in the 1992 *Pesticides in Ground Water Database*, U.S. EPA/EFED/EFGWB, and was not included in the National Pesticide Survey, USEPA 1990. Therefore, the SCI-GROW screening model was used to estimate ground water concentrations. The model estimates upper-bound ground water concentrations of pesticides likely to occur when the pesticide is used at the maximum allowable rate in areas where ground water is vulnerable to contamination.

The SCI-GROW model estimated the concentration of difenoconazole in drinking water from shallow ground water sources to be **0.0012 µg/L.** This concentration can be considered as both the acute and chronic value. Since SCI-GROW is not designed to estimate leaching from seed treatment pesticides, there are uncertainties associated with the SCI-GROW estimated groundwater concentration.

Table 4. SCI-GROW Input Parameters for the Use of Difenoconazole on Wheat		
MODEL PARAMETER	DATA SOURCE	VALUE
Application Rate On Wheat	Label EPA Reg# 100-788	0.03 lb ai/Acre (based on 125 lb seeding/Acre)
Koc	42245135	3693 ml/g (median value)
Aerobic Soil Metabolism $t_{1/2}$	42245130	1600 days

IV. Aquatic Organisms Risk Assessment

In terms of acute toxicity, difenoconazole is characterized as moderately to highly toxic to both fresh water and to estuarine/marine organisms. However, the estimated risk quotients for the proposed use of difenoconazole on canola did not exceed the acute LOC's for fresh water and for estuarine/marine fish and invertebrates. Also, the risk quotients did not exceed the chronic LOC's for fresh water fish and invertebrates. The chronic risk quotients for estuarine/marine fish and invertebrates were not calculated due to the lack of acceptable chronic toxicity data for estuarine/marine organisms.

Table 4. Aquatic Organisms Predicted Risk Quotients from A Single Application of Difenoconazole As Seed Treatment for Canola					
Crop	**GENEEC estimates in ppb**	**Toxicity Values in ppb**			
Canola 1 x 0.00192 lb ai/acre seed treatment	Day 0 Day 21 Day 56	**Freshwater Fish** 96 HR LC50 = 351 83D NOEC =8.7	**Freshwater Invert.** 48 HR EC50= 770 21D NOEC =5.6	**Marine Fish** 96 HR LC50= 819 36 D NOEC= N/A	**Marine Invert.** LC50= 300 28 D NOEC= N/A
	0.0077 0.0044 0.0029	Acute RQ <0.001 Chronic RQ <0.001	Acute RQ <0.001 Chronic RQ =0.001	Acute RQ <0.001 Chronic RQ = N/A	Acute RQ <0.001 Chronic RQ = N/A

V. Terrestrial Animal Risk Assessment

Table 5 presents the toxicity data for terrestrial organisms and rat toxicity values which were obtained from the Agency's Health Effects Division (HED) to substitute for wild mammal testing.

Table 5. Terrestrial Wildlife Toxicity Data		
Common Name	**Toxicity Levels**	**MRID #**
Rat - oral acute	LD_{50} = 1453mg/kg bw	42090006
Rat - reproductive	NOAEL=25 mg/kg diet	42090018
Mallard	LD_{50} > 2150 mg/kg bw (acute oral toxicity study)	42245105
Bobwhite	LC50 = 4760 mg/kg diet (dietary toxicity study)	42245103
Mallard	LC50 > 5000 mg/kg diet (dietary toxicity study)	42245104
Mallard	NOAEC=125 mg/kg diet (avian reproductive study)	42245106
Bee	LD_{50} = 100 µg/bee (48 hr contact)	42245124

Exposure and Risk to Nontarget Terrestrial Organisms

Birds: Acute

Granular products/Seed Treatment:
Birds may be exposed to granular pesticides and seed treatments by ingesting granules or seeds when foraging for food or grit. They also may be exposed by other routes, such as by walking on exposed granules or drinking water contaminated by granules or treated seeds. The assessment below bases acute exposure on a bird diet consisting solely of difenoconazole-treated seeds. This approach defines a risk quotient (RQ) as

$$RQ= \text{seed concentration (mg/kg-diet)}/LC_{50} \text{ (mg/kg-diet)}$$

Risk is assumed to occur for any RQ value greater than 0.5. The seed treatment rate for the proposed use is 0.025 lbs a.i./100 lbs (EPA Reg. No. 100-778), which translates to a seed concentration of 11,339 mg a.i./ 45.4 kg or 250 mg a.i./kg.

RQ results for this analysis are summarized in the table below. Based on this assessment, the resultant RQs do not exceed any EFED acute levels of concern (LOCs)

Table 6. Summary of avian acute RQ evaluation.				
	Difenoconazole Seed Conc (per label)		Dietary LC_{50} Bobwhite Quail	RQ = $\frac{\text{mg a.i./kg seed}}{LC_{50}}$
Crop	lb ai/8 lb seed	mg a.i./kg seed	mg/kg-diet	
Canola	0.00192	240	4760	0.050

Birds: Chronic

To determine chronic risk to birds, the concentration on the food item (seeds) was determined from the label. Chronic RQ was calculated using the following equation:

RQ = Concentration on seeds / NOAEC.

Results are given in the table below and suggest a potential for chronic reproductive risk to avian species from the use of difenoconazole-treated seed. The RQ exceeds the EFED chronic risk LOC (1.0)

Table 7. Summary of avian chronic RQ evaluation. RQs in bold indicate potential risk

	Difenoconazole Seed Conc (per label)		Chronic Dietary NOAEC Bobwhite Quail	$RQ = \frac{\text{mg a.i./kg seed}}{LC_{50}}$
Crop	lb ai/8 lb seed	mg a.i./kg seed	mg/kg-diet	
Canola	0.00192	240	125	**1.920**

Mammals: Acute

Granular products/Seed Treatment:
Mammals may be exposed to granular pesticides ingesting granules or seeds when foraging for food or grit. They also may be exposed by other routes, such as by walking on exposed granules or drinking water contaminated by granules or treated seeds. Because available acute toxicity endpoints are expressed as oral dose (mg/kg-body weight) and not dietary concentrations, the exposure assessment must convert pesticide concentration in treated seed to an oral dose estimate. For the purposes of this risk assessment, seeds are assumed to comprise 100% of the daily diet of granivorous mammals for a short-term exposure duration.

EFED relied on an allometric relationship established for mammals that relates bodyweight to mass of food consumed (dry weight) per day (Nagy 1987)[2]. This relationship for the general case of all mammals is

$$\text{food ingestion } (kg_{dry}/\text{day}) = 0.0687\ (\text{mammal mass kg})^{0.822}$$

EFED used three weight classes of mammals (15, 35, and 1000 g mammals) to calculated estimated food ingestion rates of 2.18, 4.37, and 68.7 g (dry)/day. Using an assumption of 9%

[2]Nagy, K.A. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecol. Monogr. 57:111-128.

water content in seeds (USEPA 1993)[3], these ingestion rates expressed as fresh weight are 2.4, 4.8, and 74.9 g/day, for the 13, 35, and 1000 g mammals.

To calculate the daily oral dose of pesticide the seed concentration of pesticide, the ingestion rate, and the animal body weight are considered as follows:

$$\text{Daily dose mg a.i./kg-body weight} = \frac{(\text{Food ingestion } kg_{fresh}/\text{day})(\text{pesticide concentration mg a.i./kg food})}{\text{body weight kg}}$$

Table 8 summarizes the pesticide daily doses and resulting RQs None of the RQs exceed EFED acute LOCs.

Table 8. Summary of mammalian acute RQ evaluation.									
	Difenoconazole Seed Conc. (per label)		Dose (mg ai per /kg mammal)			Acute LD_{50}	RQ = Dose/LD_{50}		
Crop	lb ai/8 lb seed	mg ai/kg seed	0.015 kg mammal (FI = 0.0024 kg/day) [1]	0.035 kg mammal (FI = 0.0048 kg/day) [1]	1kg mammal (FI = 0.0749 kg/day) [1]	rat mg/kg-bw	0.015 kg mammal	0.035 kg mammal	1 kg mammal
Canola	0.00192	240	38.4	33.6	18.0	1453	0.026	0.023	0.012

Mammals: Chronic

To determine chronic risk to mammals, the concentration on the food item (seeds) was determined from the label. Chronic RQ value was calculated using the following equation:

$$\text{RQ} = \text{Concentration on seeds / NOAEL}.$$

The NOAEL for the rat (25 mg/kg-diet) was used as an approximation for all mammals. Results are given in Table 9 and indicate a potential for chronic reproductive risk to mammalian species from the use of difenoconazole-treated seed. The RTQ exceeds the EFED chronic risk level of concern (1.)

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[3]United States Environmental Protection Agency (USEPA). 1993. Wildlife Exposure Factor Handbook. EPA/600/R-93/187a. Office of Research and Development, Washington, DC.

Table 9. Summary of mammalian chronic RQ evaluation. RQs in bold indicate potential risk				
	Difenoconazole Seed Conc (per label)		Chronic Tpxocty endpoint	RQ = mg a.i./kg seed / NOAEL
Crop	lb ai/8 lb seed	mg ai/kg seed	Rat 2-Generation Reproduction NOAEL (mg/kg-diet)	
Canola	0.00192	240	25	**9.6**

Insects

Currently, EFED does not assess risk to nontarget insects. Results of acceptable studies are used for recommending appropriate label precautions. Difenoconazole is relatively non toxic (100 ug/bee) to honeybees. Since this is a seed treatment application, low risk is assumed to flying insects, however beneficial soil dwelling insects may be at risk.

Plants

No studies of plant toxicity have been submitted to the agency. Because difenoconazole is a fungicide, it may be assumed to be non hazardous to terrestrial plant. Fungicides may be toxic to certain aquatic plants and hence aquatic plant data are needed even though the potential for aquatic exposure from seed treatment use is minimal.

APPENDIX A: Environmental fate data for difenoconazole

1. Degradation

<u>**Hydrolysis: 161-1**</u> (Satisfied)
Study MRID 42245127
Atkins, R.H. 1991. Hydrolysis of [^{14}C]CGA-169374 at pH 5, 7, and 9. PTRL Project No. 494. Unpublished study performed by PTRL, East Inc., Richmond, KY and submitted by Ciba-Geigy, Greensboro, NC.

[^{14}C]Triazole ring-labeled difenoconazole did not hydrolyze in pH 5, 7, and 9 aqueous buffers when incubated at 25 C for 30 days. The parent compound comprised 95.2-109.0% of the initial radioactivity throughout the study (Table V). There were two unknown compounds designated A and B which comprised maximums of 1.2 and 1.1% of the initial radioactivity, respectively; the unknowns were not consistently recovered from all samples at every sampling interval. Material balances ranged from 94.9 to 114.2% of the initial radioactivity at all pH levels at each sampling interval.

<u>**Aqueous Photolysis: 161-2**</u> (Not Satisfied)
Study MRID 42245128 (Supplemental)
Spare, W. C. 1991. Aqueous photolysis of ^{14}C-CGA-169374. Agrisearch Project No: 12195. Unpublished study performed by Agrisearch Incorporated, Frederick, MD; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

Triazole ring-labeled [3,5-^{14}C]difenoconazole, at a nominal concentration of 1 ppm (actual concentration of 0.86 ppm), degraded with of 6 days (r^2 = 0.97) in sterilized pH 7 aqueous buffer solution which was irradiated with a xenon arc lamp (12 hour light/dark cycle) and maintained at 25 ± 1°C for up to 30 days. The parent compound was relatively stable in the pH 7 dark control solutions. In the irradiated solutions, the parent compound was initially 98.3% of the applied radioactivity, decreased to 55.4% by 5 days, was 15.8-16.4% from 9 to 15 days posttreatment, and was 2.3% at 30 days. The major degradate CGA-71019 was initially (day 5) 9.2% of the applied radioactivity, was a maximum of 12.9% at 9 days posttreatment, and was 8.6-11.2% from 15 to 30 days. An unidentified major degradate (Unknown 2) was 4.0-5.6% of the applied radioactivity from 1 to 3 days posttreatment, was a maximum of 19.1% at 9 days, and was 3.9-6.1% from 22 to 30 days. An unidentified major degradate (Unknown 1) was initially (day 2) 6.6% of the applied radioactivity, was a maximum of 14.0% at 5 days posttreatment, and was 0.3% at 30 days. The minor degradates CGA-205375 and CGA-205374 were present at ≤2.9% and ≤1.5% of the applied radioactivity, respectively, throughout the incubation period. Uncharacterized polar radioactivity was initially (day 2) 0.5% (one sample) of the applied radioactivity, increased to 13.5% by 5 days posttreatment, was 48.3% at 9 days, and was a maximum of 84.6% at 30 days. In the dark control solutions, the parent compound was present at 99.7-104.8% of the applied radioactivity from 0 to 22 days posttreatment, and decreased to 88.4% by 30 days. The minor degradate CGA-205374 was detected once, at 1.4% of the applied radioactivity at 5 days posttreatment.

Photodegradation on soil (161-3) (Not Satisfied)
A new study is required

2. Metabolism

Aerobic and Anaerobic Soil Metabolism 162-1,162-2 (Not Satisfied)
Study MRID 42245131 (Supplemental)
Gonzalez-Valero, J. 1991. (Interim Report) Rate of degradation of ^{14}C-CGA-169374 in aerobic soil at various conditions. Laboratory Project IDs: 91GJ01 and 91GJ02. Unpublished study performed by CIBA-GEIGY Limited, Basel, SWITZERLAND; and submitted by CIBA-GEIGY Corp., Greensboro, NC.

The study indicate that difenoconazole is moderately persistent in soil under aerobic conditions with a registrant calculated half-life (reported as a DT_{50}) of 79 days. The high treatment rate study used an exaggerated dose rate of 1.0 kg ai/ha (8 X the maximum label rate) and was terminated before the pattern of decline of the test substance was established. The low treatment rate study used a dose rate of 0.1 kg ai/ha (0.1 ppm) which is less than the maximum label rate for difenoconazole of 0.125 kg ai/ha. (0.1116 lb ai/acre)

Study MRID 42245132 (Supplemental)
Spare, W. C. 1987. Soil metabolism of CGA-169374 under aerobic, aerobic/anaerobic and sterile conditions. Laboratory Project No.: 1239. Unpublished study performed by Agrisearch Incorporated, Frederick, MD; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

The parent compound was relatively stable in both aerobic and anaerobic loam soil. The registrant-calculated half-lives for the parent in aerobic and anaerobic loam soil systems were 1600 days and 947 days, respectively.

In the aerobic soil metabolism study, radiolabeled difenoconozole, at a nominal application rate of 10 ppm, was relatively stable in aerobic loam soil that was incubated in darkness at 25 ± 1°C for up to 12 months. However, data were variable over time. Data reported percentages of the applied radioactivity represent percentages of the nominal application. Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate. The parent compound was initially present in the soil at 91.4% (9.1 ppm) of the applied radioactivity and was variable at 62.0-99.7% (6.2-10.0 ppm) at 1-365 days posttreatment. No major degradates were detected; one unidentified minor degradate was detected. Nonextractable [^{14}C]residues were initially (time 0) 2.3% (0.23 ppm) of the applied radioactivity, increased to 18.7% (1.9 ppm) by 3 months, and were 15.5% (1.6 ppm) at 12 months posttreatment (reviewer-calculated means). Evolved $^{14}CO_2$ and [^{14}C]organic volatiles were not detected.

In the anaerobic soil metabolism study, radiolabeled difenoconozole, at a nominal application rate of 10 ppm, was stable in flooded loam soil that was incubated anaerobically (nitrogen) in darkness at 25 ± 1°C for up to 61 days following a 30-day aerobic incubation period. However, data were variable throughout the 30-day aerobic incubation, and only two samples were taken after anaerobic conditions were induced. Data reported as percentages of the applied radioactivity represent percentages of the nominal application. Data were not reported in units of concentration. Time 0 data were determined prior to flooding (following 30 days of aerobic incubation). Sampling intervals are reported as days following the initiation of the anaerobic phase of the study. Total system data were not reported. The parent compound was initially present in the soil phase at 87.1% of the applied radioactivity and was 83.2-83.3% at 28-61 days. No major degradates were detected; one unidentified minor degradate was detected. Nonextractable [^{14}C]residues were initially (time 0) 8.9% of the applied radioactivity and were 21.0-21.6% at 28-61 days following the initiation of anaerobic conditions (reviewer-calculated mean). Evolved $^{14}CO_2$ and [^{14}C]organic volatiles were not measured. [^{14}C]Residues in the water phase (≤2.1% of the applied radioactivity) were not characterized.

Study MRID 42245133 (Supplemental)
Spare, W. C. 1992. Soil metabolism of CGA-169374 under aerobic, aerobic/anaerobic, and sterile conditions. Agrisearch Project No.: 1294. Unpublished study performed by Agrisearch Incorporated, Frederick, MD; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

Triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable (registrant-calculated half-life of 1059 days; r^2 = 0.69) in aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 365 days.

In the aerobic soil metabolism study, triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable (registrant-calculated half-life of 1059 days; r^2 = 0.69) in aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 365 days. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems (unless otherwise noted). Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate. The parent compound was initially 95.6% (9.6 ppm) of the applied radioactivity, was 82.2-83.0% (8.2-8.3 ppm) at 14-91days, and was 69.1% (6.9 ppm) at 365 days posttreatment. The minor degradate CGA-205374 (chemical name not reported) was initially (time 0) 0.9% (0.09 ppm) of the applied radioactivity and was 3.6% (0.36 ppm) at 365 days posttreatment (detected by only one TLC system). The minor degradate CGA 205375 was initially (time 0) 0.73% (0.073 ppm) of the applied radioactivity, was a maximum of 2.7% (0.27 ppm) at 181 days, and was 2.0% (0.2 ppm) at 365 days posttreatment. Nonextractable [^{14}C]residues were initially (time 0) 1.6% (0.16 ppm) of the applied radioactivity, increased to 6.0% (0.6 ppm) by 30 days and a maximum of 8.7% (0.87 ppm) by 181 days, and were 5.5% (0.55 ppm) at 272-365 days posttreatment. Total [^{14}C]volatiles were ≤0.9% (0.09 ppm) of the applied radioactivity throughout the incubation period.

In aerobic sterile control samples, triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable in sterile, aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 181 days. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems. Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate. The parent compound was initially 95.6% (9.6 ppm) of the applied radioactivity and was 88.7% (8.9 ppm) at 181 days posttreatment. The minor degradate CGA-205374 was present at 0.35-0.95% (0.035-0.1 ppm) of the applied radioactivity at 30-181 days posttreatment (detected by only one TLC system). The minor degradate CGA-205375 was present at 0.60-1.7% (0.060-0.71 ppm) of the applied radioactivity at 30-181 days posttreatment. Nonextractable [^{14}C]residues were 2.1-3.8% (0.21-0.38 ppm) of the applied radioactivity at 30-181 days posttreatment. Total [^{14}C]volatiles were $\leq$0.1% (0.01 ppm) of the applied radioactivity.

In the anaerobic soil metabolism study, triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable in flooded sandy loam soil that was incubated anaerobically (nitrogen) in darkness at 23.5-26.0°C for up to 61 days following a 30-day aerobic incubation period. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems. Data were not reported in units of concentration. Time-0 data were determined prior to flooding (following 30 days of aerobic incubation). Sampling intervals are reported as days following the initiation of the anaerobic phase of the study. In the total soil/water system, the parent compound was initially present at 82.6% of the applied radioactivity and was 75.7-79.7% at 29-61 days following the initiation of anaerobic conditions. In the soil phase, the parent compound was initially present at 82.6% of the applied radioactivity and was 73.1-77.2% at 29-61 days. The minor degradate CGA-205374 was initially (time 0) 1.9% of the applied radioactivity and was 3.6% at 61 days following the initiation of anaerobic conditions (detected by only one TLC system). The minor degradate CGA-205375 was initially (time 0) 1.1% of the applied radioactivity (three of four replicates) and increased to 2.5% by 61 days following the initiation of anaerobic conditions. Nonextractable [^{14}C]residues were initially (time 0) 6.0% of the applied radioactivity, were 6.2% at 29 days, and were 4.3% at 61 days following the initiation of anaerobic conditions. In the water phase, the parent compound was present at 2.5-2.7% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions. The minor degradate CGA-205374 was 0.7-0.9% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions (detected by only one TLC system). The minor degradate CGA-205375 was 0.45-1.1% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions. [^{14}C]Volatiles were not measured.

<u>Anaerobic aquatic metabolism (162-3)</u> (Not Satisfied)

Aerobic Aquatic metabolism (162-4) (Not Satisfied)

3. Mobility

Leaching and Adsorption Desorption Studies 163-1 (Not Satisfied)
Study MRID 42245135 (Supplemental)
Atkins, R. H. 1991. Soil adsorption/desorption of [^{14}C]CGA-169374 by the batch equilibrium method. PTRL Project No.: 495. CIBA-GEIGY Study No.: 114-90. Unpublished study performed by PTRL East, Inc., Richmond, KY; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

Triazole ring-labeled [3,5-^{14}C]difenoconazole (MRID 42245135), at nominal concentrations of 0.1, 0.2, 0.4, 0.7, and 1.0 ppm, was studied in sand, sandy loam, silt loam, and silty clay loam soil:solution slurries that were equilibrated for 24 hours in darkness at 25 ± 0.0°C. Freundlich K_{ads} values were 12.8 for the sand soil (0.62% o.m.), 63.0 for the sandy loam soil (3.4% o.m.), 54.8 for the silt loam soil, and 47.2 for the silty clay loam soil; corresponding K_{oc} values were 3867, 3518, 3471, and 7734 mL/g. Respective 1/N values (reviewer-calculated) were 0.74, 0.76, 0.85, and 0.91 for adsorption. Freundlich K_{des} values determined following a 24-hour equilibration period were 18.6 for the sand soil, 95.2 for the sandy loam soil, 57.2 for the silt loam soil, and 71.4 for the silty clay loam soil; corresponding K_{oc} values were 5624, 5320, 3620, and 11700 mL/g. Respective 1/N values (reviewer-calculated) were 0.75, 0.80, 0.76, and 0.93 for desorption. The reviewer-calculated coefficients of determination (r^2) for the relationships K_{ads} *vs.* organic matter, K_{ads} *vs.* pH, and K_{ads} *vs.* clay content were 0.74, 0.18, and 0.21, respectively.

Study MRID 42245136 (Supplemental)
Spare, W. C. 1988. Adsorption/desorption of ^{14}C-CGA-169374. Agrisearch Project No.: 12115. Unpublished study performed by Agrisearch Incorporated, Frederick, MD; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

Triazole ring-labeled [3,5-^{14}C]difenoconazole (MRID 42245136), at nominal concentrations of 0.02, 0.05, 0.1, 0.5 and 1.0 µg/mL, was studied in autoclave sterilized clay, sand, silt loam, and sandy loam soil:solution slurries that were equilibrated for 8 hours at 25 ± 1°C. Freundlich K_{ads} values were 97.9 for the clay soil (4.8% o.m.), 2.1 for the sand soil (0.9% o.m.), 35.0 for the silt loam soil, and 11.5 for the sandy loam soil; corresponding K_{oc} values were 3466, 400, 5663, and 1956 mL/g. Respective 1/N values (reviewer-calculated) were 0.89, 0.80, 0.88, and 0.94 for adsorption. Freundlich K_{des} values determined following a 8-hour equilibration period were 119.1 for the clay soil, 4.2 for the sand soil, 66.7 for the silt loam soil, and 17.3 for the sandy loam soil; corresponding K_{oc} values were 4217, 790, 10792, and 2939 mL/g. Respective 1/N values (reviewer-calculated) were 0.86, 0.85, 0.89, and 0.94 for desorption. The reviewer-calculated coefficients of determination (r^2) for the relationships K_{ads} *vs.* organic matter, K_{ads} *vs.* pH, and K_{ads} *vs.* clay content were 0.91, 0.36, and 0.93, respectively.

Laboratory Volatility from Soil (163-2) (Not Satisfied)

Field Volatility (163-3) (Not Satisfied)

4. Dissipation

Terrestrial Field Dissipation Studies 164-1 (Not Satisfied)
Study MRID 42245140 (Supplemental)
Kimmel, E. C. 1992. Mobility and dissipation of [^{14}C-Phenyl]-CGA-169374 under actual field conditions. PTRL-West Project No.: 111W. Unpublished study performed by PTRL-West, Inc., Richmond, CA; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

Uniformly phenyl ring-labeled [^{14}C]difenoconazole (CGA-169374), applied at a nominal application rate of 51.8 g a.i./A (0.41 mg/lysimeter) to lysimeter-enclosed bareground plots of loamy sand soil in Reedley, California, dissipated with a registrant-calculated half-life of 252 days (r^2 = 0.91); however, the observed first half-life occurred between 93 and 182 days posttreatment. The half-life was determined from the parent detected in the 0- to 3-inch depth rather than the top 6 inches. Data are reported as percentages of the nominal application and are reviewer-calculated means of methanol:water plus oxalic acid:DMF extractions. Residue data were only reported for the 0- to 3-inch depth. The parent was initially 82.4% (0.1 ppm) of the applied radioactivity in the 0- to 3-inch depth, decreased to 49.7% (0.072 ppm) by 93 days posttreatment, and was 25.7% (0.03 ppm) at 363 days. Degradate data are reported in parent equivalents. The minor degradate CGA-190978 was a maximum of 1.3% (0.001 ppm; methanol:water extraction only) of the applied radioactivity at 61 days posttreatment and was 0.59% (0.001 ppm) at 363 days. The minor degradate CGA-189138 was a maximum of 2.7% (0.003 ppm) of the applied radioactivity at 61 days posttreatment and was 1.7% (0.002 ppm) at 363 days. The minor degradate CGA-205374 was a maximum of 3.3% (0.003 ppm; methanol:water extraction only) of the applied radioactivity at time 0 and was 1.2% (0.001 ppm) at 363 days. The minor degradate CGA-205375 was a maximum of 6.9% (0.009 ppm) of the applied radioactivity at 182 days posttreatment and was 6.6% (0.008 ppm) at 363 days. [^{14}C]Residues were not characterized below the 0- to 3-inch depth. In the 3- to 6-inch depth, total [^{14}C]residues were initially 0.56% (0.001 ppm) of the applied radioactivity at 7 days posttreatment, increased to a maximum of 5.1% (0.005 ppm) by 272 days, and were 2.5% (0.003 ppm) at 363 days. In the 6- to 9-inch depth, total [^{14}C]residues were $\leq$0.94% (0.001 ppm) of the applied radioactivity from 14 to 363 days posttreatment. In the 9- to 12-inch depth, total [^{14}C]residues were 0.26-0.47% (0.0003-0.0004 ppm) of the applied radioactivity from 182 to 363 days posttreatment. In the 12- to 18-inch depth, total [^{14}C]residues were 0.30-1.3% (0.0001-0.0006 ppm) of the applied radioactivity from 182 to 363 days posttreatment. Total [^{14}C]residues detected in the leachate were 0.36% of the applied radioactivity throughout the study period.

5. Accumulation

<u>Laboratory Accumulation in Fish: 165-4</u> (Satisfied)
Study MRID 42245142
Fackler, P.H. 1991. Bioconcentration and elimination of [^{14}C]-residues by Bluegill (Lepomis macrochirus) exposed to CGA-169374. Laboratory Project ID #1781.0387.6139.140. Unpublished study performed by Springborn Laboratories Inc., Ciba-Geigy Corp., and Battelle and submitted by Ciba-Geigy, Greensboro, NC.

[^{14}C]Difenoconazole accumulated rapidly in edible and non-edible bluegill sunfish tissues with bioconcentration factors of 170x for edible tissues, 570x for nonedible tissues, and 330x for whole body. Depuration was also rapid with a depuration half-life of approximately 1 day and 96-98% clearance after 14 days of depuration. One main metabolite, CGA-205375, was recovered from both the edible and non-edible tissues and accounted for 51-64% of the applied radioactivity. There were up to 9 minor metabolites which were not identified.

There are potentially up to 9 unidentified degradates associated with fish tissues. In the edible tissues the residues ranged from 0.012 to 0.022 ppm and in the nonedible tissues the residues ranged from 0.014 to 0.74 ppm. Due to use pattern of difenoconazole as a seed treatment, the low amounts of accumulation in fish tissues, and the rapid depuration of difenoconazole, at this time EFGWB does not consider that these degradates will be of environmental concern. If degradates of difenoconazole are found to be of toxicological concern, these fish tissue metabolites should be further investigated.